Notice of Allowability	Application No.	Applicant(s)	
	10/804,470	STENDER ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment of May 2, 2007*.

2. ☒ The allowed claim(s) is/are *1-21 and 39*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *7/16/07* .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Stephana Patton on July 16, 2007.

The claims have been amended as follows:

1. A method for the analysis of a target nucleotide sequence of interest in a sample, said method comprising:

a. contacting the sample with at least one pair of probes (Probe A and Probe B),

b. hybridizing Probe A and Probe B to the sample under hybridization conditions in which the desired degree of discrimination is achieved for an accurate result, wherein:

i) Probe A comprises a nucleotide sequence which hybridizes under said hybridization conditions to both a target nucleotide sequence of interest and to a nucleotide sequence not of interest, and is labeled with a first fluorophore;

ii) Probe B comprises a nucleotide sequence which hybridizes under said hybridization conditions to a nucleotide sequence not of interest adjacent the nucleotide sequence not of interest to which Probe A hybridizes, and is labeled with a quencher;

c. detecting the hybridization of Probe A, wherein the fluorescence generated by the hybridization of Probe A to the nucleotide sequence not of interest is quenched by hybridization of probe B to the nucleotide sequence not of interest, and

d. correlating the presence or amount of target nucleotide sequence of interest in the sample with the fluorescence generated upon hybridization of Probe A to the target nucleotide sequence of interest, wherein detection of the fluorescence of the fluorophore of Probe A is an indication of the presence or amount of the target nucleotide sequence of interest in said sample.

10. The method of claim 1, wherein Probe A consists of the following nucleotide sequence: GCT-TCT-CGT-CCG-TTC (SEQ ID NO: 1) and the fluorophore.

11. The method of claim 1, wherein Probe B consists of the following nucleotide sequence: ACT-TCA-AAG-GAG-CAA (SEQ ID NO: 1) and the quencher.

12. The method of claim 1, wherein Probe A is labeled with the fluorophore at a terminus closest to a hybridization site of Probe B, and Probe B is labeled with a quencher at a terminus closest to a hybridization site of Probe A.

14. The method of claim 1, wherein Probe B further comprises a fluorophore at an opposite end from the quencher and wherein the fluorophore of Probe B comprises a different emission spectrum than the fluorophore of Probe A.

19. The method of claim 1, wherein step (d) of the method detects, identifies, or quantitates the presence or amount of at least one species of a microorganism in the sample.

20. The method of claim 19, wherein the target nucleotide sequence is from a microorganism exposed to at least one antimicrobial agent and the presence or amount of target nucleotide sequence of interest is indicative of an effect of the antimicrobial agent on the microorganism.

21. The method of claim 1, wherein the presence or amount of the target nucleotide sequence of interest is indicative of a condition of medical interest.

39. The method of claim 1, wherein the hybridization of Probe B increases the specificity of the analysis of the target nucleotide sequence of interest.

The following is an examiner's statement of reasons for allowance:

The closest prior art of Schutz (Clinical Chemistry. 2000. 46:1728-1737; see Figures 2 and 3, page 1730 and page 1732, col. 2) teaches a method to detect target nucleic acid sequences, wherein the method comprises a) hybridizing a first probe and a second probe to a nucleic acid sample, wherein the first probe is labeled with a fluorophore (i.e., "Probe A") and the second probe is labeled with the quencher TAMRA (i.e., "Probe B"), and b) detecting the hybridization of probe A to target nucleic acid sequences under suitable hybridization conditions. Hyldig-Nielsen (PGPUB 2002/0090626; see, e.g., para [0014]) discloses a method for detecting organisms of a genus or species wherein the method utilizes two probes that are selected so as to minimize false positive results. In the method of Hyldig-Nielson, a nucleic acid sample is contacted with a first probe that hybridizes to a target nucleic acid of interest and which may also cross hybridize to nucleic acids not of interest, and with a second probe which specifically hybridizes to

nucleic acids not of interest. Detection of hybridization of the first probe in the absence of hybridization of the second probe is indicative of the presence of the target nucleic acid of interest. Hyldig-Nielson does not teach that the first probe is labeled with a fluorophore and the second probe is labeled with a quencher and that the first and second probes hybridize adjacent to one another on the nucleic acid sequence not of interest, such that hybridization of the first and second probes together results in quenching of the fluorescence generated by the first probe. Accordingly, the prior art does not teach or suggest the presently claimed method for the analysis of a target nucleotide sequence of interest wherein the method comprises contacting a nucleic acid sample with a Probe A and Probe B under hybridization conditions, wherein Probe A comprises a nucleotide sequence which hybridizes under said hybridization conditions to both a target nucleotide sequence of interest and to a nucleotide sequence not of interest and is labeled with a first fluorophore, and Probe B comprises a nucleotide sequence which hybridizes under said hybridization conditions to a nucleotide sequence not of interest adjacent the nucleotide sequence not of interest to which Probe A hybridizes and Probe B is labeled with a quencher;
detecting the hybridization of Probe A, wherein the fluorescence generated by the hybridization of Probe A to the nucleotide sequence not of interest is quenched by hybridization of probe B to the nucleotide sequence not of interest; and correlating the presence or amount of target nucleotide sequence of interest in the sample with the fluorescence generated upon hybridization of Probe A alone to the target nucleotide sequence of interest, wherein detection of the fluorescence of the fluorophore of Probe

A is an indication of the presence or amount of the target nucleotide sequence of interest in said sample.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Carla Myers/
Primary Examiner, Art Unit 1634